GT

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,764	02/04/2004	Daniel Achard	USST00008US CNT1	3675

5487 7590 02/23/2006

ROSS J. OEHLER
AVENTIS PHARMACEUTICALS INC.
ROUTE 202-206
MAIL CODE: D303A
BRIDGEWATER, NJ 08807

EXAMINER	
RAO, DEEPAK R	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 02/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/771,764	ACHARD ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/798,589.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *020404 & 083004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-6 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating pain, does not reasonably provide enablement for a method of treating all the disorders that respond to treatment with cannabinoid antagonists selected from schizophrenia, Parkinson's disease, Huntington's chorea, Raynaud's syndrome, and alcohol abuse. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The instant claims are drawn to 'a method for the treating a disorder..... selected from schizophrenia, Parkinson's disease, Huntington's chorea, Raynaud's syndrome, and alcohol abuse'. The instant claim language covers diseases that are very difficult to treat, e.g., schizophrenia, alcohol abuse, etc. Substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or "not provided", see *Ex parte Jovanovics*, 211 USPQ 907, 909.

The activity for the compounds disclosed in the specification is as cannabinoid receptor antagonists, useful to treat a wide list of diseases, which include various disorders, which in turn include specific diseases such as Alzheimer's disease, etc. Biological assay is provided in the specification at pages 23-24 and it is concluded that the representative compounds of formula (I) demonstrated antagonistic activity with ED_{50} <50 mg/kg, however, there is nothing in the disclosure regarding how this *in vitro* data correlates to the treatment of the diverse disorders embraced the instant claims. Many of the claimed disorders, e.g., schizophrenia, alcohol abuse, etc., have been proven to be extremely difficult to treat. Further, there is no reasonable basis for assuming that the claimed compounds can treat the laundry list of diseases recited in the claim having diverse mechanisms.

It is known that antipsychotic medications are used to reduce the psychotic symptoms of schizophrenia. The state of the art of such antipsychotic drugs, however, indicates that 'they do not cure or restrain the symptoms of schizophrenia or ensure that there will be no further psychotic episodes'. The online information about the treatment options of the disease http://www.psychologyinfo.com/schizophrenia/medication-treatment.html indicates that 'it is difficult to predict which patients will benefit from treatment with antipsychotic drugs. Different

patients have different treatment responses and side effects to various antipsychotic drugs', thus, clearly indicating the unpredictability in the dosage regimen.

The instant claims specifically recites 'a method for the treatment of alcohol abuse' - the scope of these claims is beyond what has been established for such a treating effect. Abuse of the use of alcohol involves different parts of the CNS system; different receptors in the body. There have been many efforts at diagnostic approaches to alcoholism. All attempts to find a pharmaceutical to treat alcohol abuse generally have not been successful. The biological mechanism of alcoholism is unknown, although the biologic mechanism of alcohol metabolism and alcohol-induced behavioral change is well-described in the literature. Alcohol itself is not a factor in the development of this condition, however, or one would be able to turn a non-alcoholic into an alcoholic through the provision of alcohol (the literature has demonstrated that this is impossible). Because addiction has so many dimensions and disrupts so many aspects of an individual's life, treatment for this illness is never simple.

Applicant has not provided any reference(s) that forms sufficient evidence that claimed uses were art-recognized based on activity relied on at the time of applicants' effective filing date. MPEP 2164.05(a). When the best efforts have failed to achieve a goal, it is reasonable for the PTO to require evidence that such a goal has been accomplished, *In re Ferens*, 163 USPQ 609. Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2nd 1001, 1006.

The diagnosis of each of the disease is generally suggested by medical history and reports of endoscopy, cytology, X-ray, biopsy, etc. depending on the symptoms, signs and complications, which is essential to establish the dosage regimen for appropriate treatment. The disclosure does not provide any guidance towards the dosage regimen required to facilitate the treatment and/or inhibition of the claimed disorders, nor indicate competent technical references in the appropriate methods.

(Only a few of the claimed diseases are discussed here to make the point of an insufficient disclosure, it does not definitely mean that the other diseases meet the enablement requirements).

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use in treating disorders selected from schizophrenia, Parkinson's disease, Huntington's chorea, Raynaud's syndrome, and alcohol abuse.

2) The state of the prior art: There are no known single group of compounds of similar structure which have been demonstrated to treat the wide variety of disorders instantly recited.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously

varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Pertwee, in a recent article regarding cannabinoid receptor ligands (Tocris Reviews, 2001) concluded that "... many important questions still remain unanswered or incompletely addressed so prompting the need for more research at both non-clinical and clinical levels", see page 7, col. 2. Therefore, the state of the art provides the need of undue experimentation for the instantly claimed therapeutic benefits.

4) The amount of direction or guidance present and 5) the presence or absence of working examples: There are no doses present to direct one to protect a potential host from the disorders nor there are doses given for the treatment of the disorders commensurate in scope with the claims.

6) The breadth of the claims: The instant claims embrace the treatment of disorders selected from schizophrenia, Parkinson's disease, Huntington's chorea, Raynaud's syndrome, and alcohol abuse.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have

to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,734,176. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims substantially overlap the reference claims. The reference claims are drawn to 'a method of treating a disorder that responds to treatment with cannabinoid antagonists' using compounds of formula (I) and the disclosure provides that the disorders include pain, schizophrenia, Parkinson's disease, Huntington's chorea, Raynaud's syndrome, alcohol abuse, etc., see col. 10,

lines 8-26. The instant claims differ by reciting specific disorders. It would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the disorders embraced by the genus taught by the reference, including those instantly claimed, because the skilled chemist would have the reasonable expectation that the compounds to have the same activity and therefore useful in treating the disorders taught in the reference. One of ordinary skill in the art would have been motivated to use the cannabinoid antagonists taught by the reference in the treatment of the specific disorders of the instant claims because such therapeutic method would have been suggested by the reference claims.

Receipt is acknowledged of the Information Disclosure Statements filed on February 4 and August 30, 2004 and copies are enclosed herewith.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deepak Rao
Primary Examiner
Art Unit 1624

February 21, 2006